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(REVIEW ARTICLE)

# Invasomes: A vesicular carrier for transdermal delivery

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## Abstract

The transdermal route serves as a crucial pathway for delivering localized or systemic medications. Recognizing the skin's significance as a vital organ, it is imperative to develop effective strategies for drug delivery through this route. Invasomes represent a novel vesicular system that has shown superior transdermal penetration compared to traditional liposomes. Comprising phospholipids, ethanol, and terpene, invasomes exhibit suitable transdermal penetration properties for soft vesicles. These nanovesicles enhance drug permeability into the epidermis while minimizing systemic absorption, thereby confining drug action within the skin subcaste. In comparison to liposomes and ethosomes, invasomes penetrate deeper into the skin. They offer various advantages, including enhancing medication efficacy, improving patient compliance, and enhancing comfort. The ability to access the skin subcaste enhances the effectiveness of invasomes, which exert their effects by fluidizing the bilayer structure of stratum corneum (SC) lipids and disrupting lipid and intracellular protein interactions. These recently discovered vesicles are tailored for use in topical and transdermal drug delivery due to their saturation effect and high deformability, distinguishing them from transferosomes.

**Keywords:** Invasomes; Terpenes; Transdermal penetration; Transferosomes; Vesicles

## 1. Introduction

Transdermal drug delivery systems offer an alternative route of administration to the systemic circulation, bypassing the need for oral ingestion or injection. The outermost layer of the skin, known as the stratum corneum, acts as the primary barrier, shielding the skin from potentially harmful environmental agents while also preventing excessive moisture loss to the external environment. Within the stratum corneum, intercellular lipids play a crucial role in maintaining the skin's homeostasis, contributing to its overall integrity and protective function[1]. Transdermal drug delivery facilitates the direct introduction of bioactive molecules into the systemic circulation, offering advantages such as bypassing hepatic metabolism, enhancing patient compliance, and reducing the risk of tissue injury. This approach represents a significant advancement in pharmaceutical delivery, providing a convenient and effective means of administering medication while minimizing potential side effects associated with other routes of administration [1-2]. The utilization of transdermal drug delivery is experiencing rapid growth in formulation development as it enhances the bioavailability of numerous drugs. However, when drugs are administered via the transdermal route, they can adversely affect the skin barrier. This impact underscores the importance of careful consideration and formulation optimization to mitigate potential harm while maximizing therapeutic efficacy [2-3]. In recent years, vesicular systems have garnered significant attention as potential drug carrier systems for both dermal and transdermal drug administration. The exploration of novel drug delivery systems is crucial to expanding the range of drugs viable for transdermal administration. Various physical methods, such as iontophoresis, sonophoresis, microneedles, and penetration enhancers, along with chemical processes utilizing liposomes, invasomes, transferosomes, and ethosomes, have demonstrated effectiveness in enhancing drug permeability through the stratum corneum. These diverse

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approaches offer promising avenues for improving the efficiency and versatility of transdermal drug delivery, thereby advancing therapeutic outcomes and patient care [4-8].

Liposomal vesicular systems offer the flexibility to incorporate both lipophilic and hydrophilic drugs, aiding in the penetration of the incorporated agents. Novel elastic vesicles, which include penetration enhancers, surpass conventional liposomes due to their enhanced interaction with the skin and improved drug penetration capabilities. This advancement holds promise for enhancing the effectiveness of drug delivery systems, potentially leading to improved therapeutic outcomes and patient experiences in various medical applications [1,2].

Over the past two decades, several researchers have introduced new classes of lipid vesicles, each contributing to advancements in drug delivery technology. Among the more recent developments, researchers have focused on investigating a novel type of vesicular system known as Invasomes. These innovative vesicles represent a promising frontier in drug delivery research, offering unique properties and potential applications in enhancing drug permeation and efficacy. The exploration of Invasomes underscores the ongoing evolution and diversification of lipid-based vesicular systems, paving the way for improved therapeutic interventions and pharmaceutical formulations [9].

Invasomes, characterized as tiny liposomal vesicles, utilize ethanol, terpenes, or terpene mixtures as potential carriers to enhance skin penetration. Compared to liposomes and ethosomes, invasomes demonstrate a higher penetration rate into the skin. This increased efficacy in permeating the skin makes invasomes a promising option in various applications[10]. Invasomes represent innovative elastic phospholipid vesicles comprising phosphatidylcholine, ethanol, and one or more terpene mixtures. Numerous researchers have validated their capacity to augment percutaneous terpenes penetration. This enhancement mechanism involves disrupting lipids in the stratum corneum, interacting with intracellular proteins, and improving drug partitioning into the stratum corneum. Ethanol further enhances the vesicles' ability to penetrate the stratum corneum, collectively making invasomes a promising avenue for various applications in dermatology and transdermal drug delivery [11].

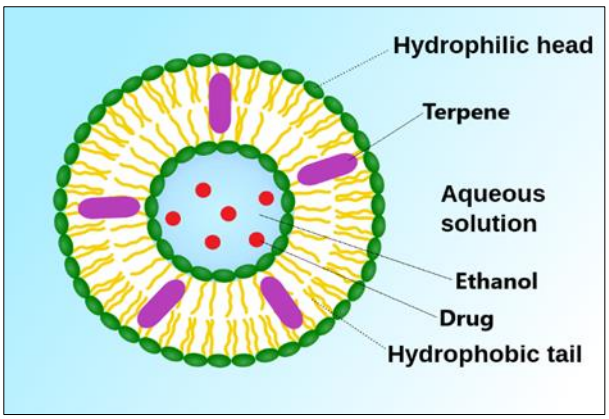


**Figure 1** Invasome Structure

Terpenes, typically natural volatile oils, are generally recognized as safe substances, especially at lower concentrations (1-5%), without causing irritation. Their reversible effects on the lipids of the stratum corneum make them clinically acceptable penetration enhancers. The synergistic impact of terpenes and ethanol on percutaneous absorption has been notably observed, suggesting their potential in enhancing transdermal delivery and formulation development [12].

According to the literature, invasomes consist of a combination of phosphatidylcholine, ethanol, and terpenes/terpenoids, each playing crucial roles in their functionality. Phosphatidylcholine contributes to bilayer formation, while lysophosphatidylcholine aids in edge activation. Ethanol facilitates improved penetration, alongside terpenes. Notably, the bilayer components confer either "stiffness" or "fluidity" to the vesicles, highlighting their dynamic nature and versatility in various applications within drug delivery and skincare formulations [2].

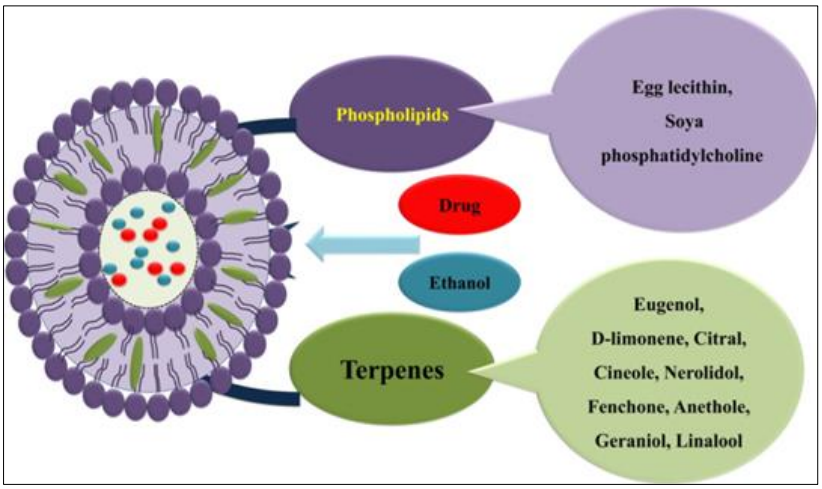


**Figure 2** Composition of Invasomes

### 1.1. Advantages of invasomes

- It is a non-invasive drug delivery technique.
- Better patient compliance.
- It is more stable than other ultra-deformable vesicles.
- The formulation contains no toxic raw materials.
- Targeted drug delivery of hydrophilic and lipophilic drugs is possible.
- It can easily penetrate through skin layers.
- Compared to iontophoresis or phonophoresis and with other complicated techniques, this is simple method for the delivery of the drugs.
- Patient compliance is better as the drug can be administered as semisolid form (gel or cream) [11,12].

## 2. Methods of preparation

There are mainly two methods which are used for the preparation of the invasomes, they are as follows:

- Mechanical dispersion method
- Thin film hydration method

### 2.1. Mechanical Dispersion Technique

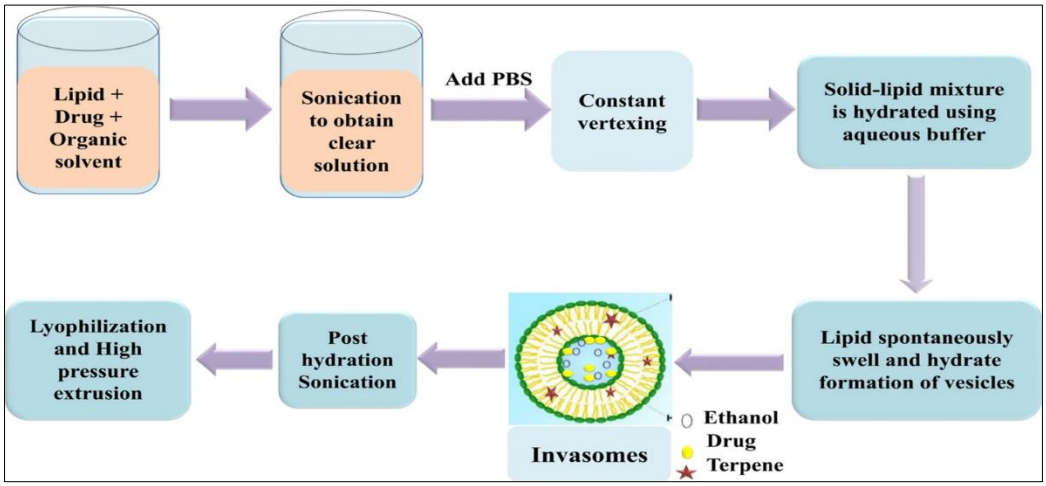


**Figure 3** Mechanical dispersion technique

To prepare the final invasomes formulation, begin by dissolving the active ingredient and terpene or terpene mixture in an ethanolic phospholipid solution. Vortex the mixture for 5 minutes and then sonicate for 5 minutes to achieve a clear solution. Following sonication, add phosphate buffered saline (PBS) with a pH of 7.4 to the solution while maintaining constant vortexing using a syringe. Continue vortexing for an additional 5 minutes to ensure thorough mixing and obtain the final invasomes preparation. This stepwise process ensures the proper encapsulation of the active ingredient within the invasomes, facilitating its delivery and potential efficacy in various applications showed in Fig 3[10].

### 2.2. Thin Film Hydration Technique

In the film hydration method, a mixture of ethanol and phospholipids is dissolved in a mixture of methanol and chloroform (2:1 v/v). The resulting mixture is then dried for 2 hours at 50°C under reduced pressure (500-1 mbar) using a rotary evaporator. Subsequently, the film is subjected to a pressure of 1 mbar for 2 hours with a nitrogen purge. To hydrate the deposited film for 30 minutes, either PBS (pH 7.4) or a mixture of terpenes, ethanol, and PBS can be chosen. Upon cooling the mixture, terpenes or a mixture of terpenes and ethanol are added to obtain invasome vesicles. The prepared invasomes are captured by vortexing, sonication, and repeated extrusion onto polycarbonate membranes with different pore size ranges. This method ensures the formation of invasome vesicles with controlled properties suitable for various applications in drug delivery and biotechnology. Formation of invasomes by membrane hydration method is shown in Fig 4[2].

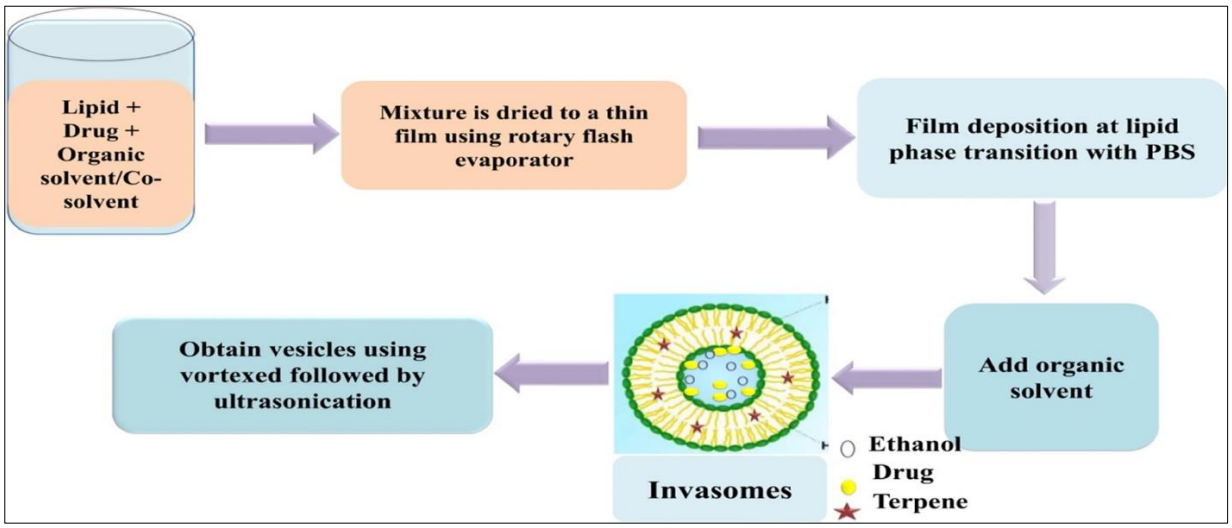


**Figure 4** Thin film hydration technique

## 3. Characterization of invasomes

- Entrapment Efficiency
- Surface Morphology
- Drug Content
- Vesicular size
- Ex Vivo Permeation Studies
- Stability Studies

### 3.1. Entrapment Efficiency

The trapping efficiency was investigated utilizing ultracentrifugation. For this, 0.1 ml of the invasomal preparation was transferred to Eppendorf tubes and centrifuged at 15,000 rpm at 4°C for 15 minutes, repeated for two cycles to isolate untrapped drugs. The transparent portion obtained after centrifugation was utilized to determine the concentration of free drug. The percentage of trapped drug was indirectly calculated based on the amount of free drug using a specific formula. This method allows for the quantification and assessment of the efficiency of drug entrapment within the invasomal vesicles, providing valuable insights for drug delivery and formulation optimization.

$$\text{Entrapment Efficiency (\%)} = \text{total drug} - \text{free total drug} \times 100$$

### 3.2. Surface Morphology

The evaluation was conducted by applying a drop of the preparation onto a transparent, air-dried glass slide coated with gold using a sputter coater and subsequently visualizing it under a scanning electron microscope. The samples were then tightly sealed in 10 ml glass vials and stored under refrigeration (4 - 8°C) and at room temperature for one month. Throughout this period, the trapping efficiency and visual appearance were regularly assessed. This method ensures the stability and integrity of the formulation over time, providing crucial insights into its long-term storage characteristics and potential applications in various fields.

### 3.3. Drug Content

The drug content within invasomes can be assessed using an ultraviolet spectrophotometer, which enables precise quantification. Additionally, an enhanced high-performance liquid chromatography (HPLC) method allows for more accurate and sensitive determination of the drug content. These analytical techniques provide valuable tools for researchers and pharmaceutical scientists to ensure the consistency and quality of invasome formulations, facilitating their development and optimization for various therapeutic applications [10].

### 3.4. Vesicular Size & Shape

Invasomes can be observed using both transmission electron microscopy (TEM) and scanning electron microscopy (SEM) techniques, offering insights into their structural characteristics and morphology. Additionally, the vesicle size and potential zeta particle size of invaginations within invasomes can be precisely determined through dynamic light scattering (DLS) and photon correlation spectroscopy methods. These analytical approaches provide comprehensive data on the size distribution and surface charge of invasomes, aiding in the optimization of their formulation and understanding their behavior in various applications, including drug delivery and biomedical research.

### 3.5. *Ex-vivo* Permeation studies

The osmolarity of the invasome formulations was assessed using a Franz diffusion cell setup. The diffusion cell, with an effective surface area of 2.0 $cm^2$ and a receptor volume of 20 ml, was utilized for the experiment. The skin was mounted onto the receiving compartment, with the stratum corneum side facing upwards, while the donor compartment was filled with the invasome preparation. A cap covered the top of the diffusion cell to maintain the experimental conditions. Phosphate-buffered saline at pH 7.4, kept at 37°C, served as the recipient medium with a volume of 20 ml. Throughout the experiment, aliquots were periodically withdrawn and replaced with fresh medium to ensure optimal conditions. The samples collected were analyzed using a UV spectrophotometer to quantify the osmolarity of the invasome formulations accurately [14].

### 3.6. Stability Studies

The physical stability of the optimized formulation was assessed to investigate drug leaching from the vesicles. The invasome gel samples were sealed in two 10 ml ointment tubes, with one tube stored in the refrigerator at 4°C to 8°C and the second tube maintained at 27°C-30°C, representing environmental temperature conditions. Over the course of one month, the samples were monitored weekly to evaluate any changes in form, drug content, and viscosity. This systematic evaluation helps ascertain the formulation's robustness and suitability for storage under different temperature conditions, providing insights into its shelf-life and stability profile [15].

## 4. Invasomes in comparison with liposomes:

Liposomes represent phospholipid-based vesicular structures comprising anionic, cationic, neutral lipids, and cholesterol, facilitating enhanced encapsulation of lipophilic, hydrophilic, and amphiphilic drugs. Within liposomes, lipophilic drugs reside in the lipid bilayer, hydrophilic drugs in the aqueous core, and amphipathic types in the middle layer of the vesicle. In contrast, invasomes are flexible liposomes consisting of phospholipids, ethanol, and a terpene molecule or mixture of terpenes. The inclusion of ethanol enhances lipid fluidity within the vesicle, resulting in a softer, less rigid structure compared to conventional liposomes, thereby improving skin permeability. Similarly, terpenes have demonstrated efficacy in enhancing penetration by disrupting the tight structure of stratum corneum lipids. These distinct characteristics and mechanisms underline the potential of invasomes as effective carriers for transdermal drug delivery, offering advantages over traditional liposomal formulations [16,17].

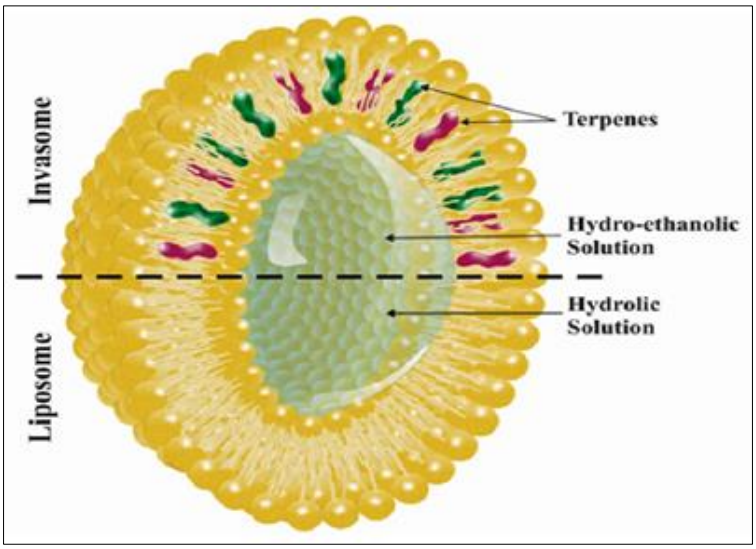


**Figure 5** Comparison structure of Invasomes and Liposomes

### 4.1. Penetration Mechanism of Invasomes

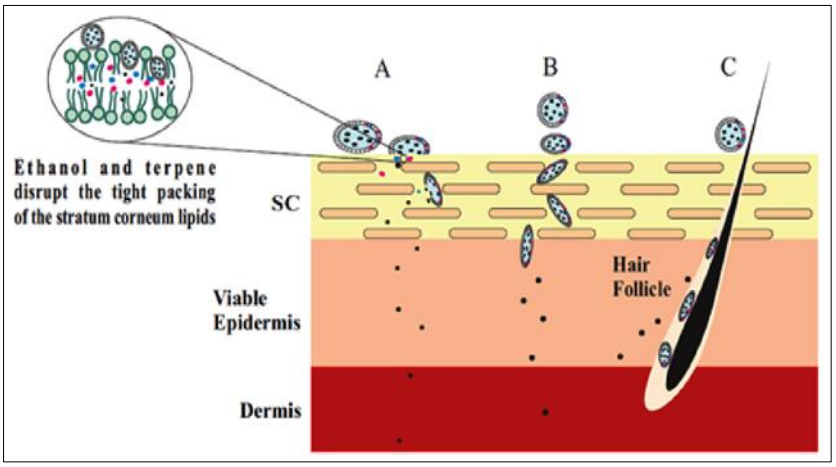


**Figure 6** Penetration mechanism of invasomes through the stratum corneum (SC). Enhanced penetration (A), intact penetration (B), and trans-appendageal penetration (C)

Terpenes and ethanol present in invasomes induce vesicle deformation, disrupt the stratum corneum (SC) bilayer backbone, and serve as penetration enhancers, thus augmenting invasome permeability. According to Dragicevic-Curic et al., upon infiltration into the skin, a portion of the invasome degrades and releases its constituents, including terpenes, phospholipid fractions, and unique toxic phospholipid molecules, facilitating SC penetration enhancement and lipid liquefaction. Invasome vesicles, being smaller and more resilient, can penetrate intact through the SC without disintegration. Verma and his group noted that upon invasion, intact invasomes can access the internal part of the SC via the follicular transport pathway or narrow hydrophilic channels within the intercellular space of the SC region. In general, while some invasomes disintegrate upon SC penetration, smaller and more flexible invasomes remain intact and can penetrate deeper layers effectively, highlighting their potential as promising carriers for transdermal drug delivery [2,19].

## 5. Applications of invasomes

An overview of various studies on the therapeutic applications and skin permeability enhancement of invasomes is given respectively [10,12]:

**Table 1** Therapeutic applications

| Drug | Applications | Type of study | Study outcomes |
|---|---|---|---|
| Avanafil | Treatment of erectile dysfunction | Excised abdominal rat skin | Optimized invasomal film improved the bioavailability and transdermal permeation of avanafil |
| Temoporfin | Photodynamic therapy (a pilot study) | Mice skin | Temoporfin invasomes containing a 1% terpene mixture decreased tumour size significantly by photodynamic therapy compared to control groups |
| Idebenone azelaic acid | Antioxidant/anticancer, anti-acne | Excised human skin | Leciplex exhibited higher permeation of idebenone and invasomes exhibited higher permeation of azelaic acid |
| Curcumin | Anti-inflammatory, antioxidant and anticancer activity | Shed snake skin | Physicochemical characteristics of the formulations influenced by terpene and tween 20 |
| Curcumin | Anti-inflammatory, anti-carcinogenic, etc | Excised rat skin | Invasome with 0.5% limonene improved intradermal penetration of curcumin |
| Temoporfin | Photodynamic therapy | Human epidermoid tumour cell line A431 | In the A431 cells temoporfin loaded invasomes were more cytotoxic |
| Temoporfin | Photodynamic therapy | Abdominal human skin | Invasomal formulation with 1% mixture of terpenes exhibited a significantly enhanced deposition of temoporfin in the SC compared to liposomes |
| Ferulic acid | Antioxidant effect | Excised human skin | Ethosomes are better vesicular carriers for the delivery of ferulic acid into the skin than invasomes |

**Table 2** Enhanced skin permeability of invasomes [10]

| Drug | Applications | Type of study | Study outcomes |
|---|---|---|---|
| Nitroxide TEMPO | Measuring the antioxidant capa | Excised human skin/excised porcine skin | Invasomes improved measurement times of antioxidative capacity by two-fold |
| Fluorescent label | Tracking of invasomes | Excised human skin, human forearm skin | Strong spectroscopic evidence shows deep penetration of intact invasomes in the SC |
| Temoporfin | Photosensitizer | ESR measurements | Terpenes improved the fluidity of the bilayers, whereas temoporfin reduced the fluidity. Therefore, invasomes represent vesicles with excessive membrane flexibility |
| 3-carboxy-2,2,5,5-tetramethyl-1 pyrrolidinyloxy (PCA) | Spin-labelling compound | Excised porcine skin | PCA permeation was improved 2.5-fold for CMS and two-fold for invasomes in comparison with PCA solution |

| | | | |
|---|---|---|---|
| Carboxyfluorescein temoporfin | Hydrophilic model drug, lipophilic model drug | Excised human skin | Ethosomes and invasomes increased the delivery of hydrophilic drug, for example carboxyfluorescein, into the deep layers of skin |
| Calceinecarboxyfluoscein | Low molecular weight hydrophilic model drugs | Excised human skin | Calcein penetration improved two and seven folds by transferosomes and invasomes respectively |

## 6. Pharmaceutical applications of invasomes

### 6.1. Delivery of vitamin analog

In recent experiments by Dwivedi and co-workers, the synthesis of isotretinoin invasomes was achieved using a mechanical dispersion method. Initially, eugenol dissolved in isotretinoin was added to ethanolic egg lecithin and vortexed for 60 minutes to achieve a homogeneous suspension. Subsequently, vesicles were hydrated using PBS (pH 6.8) to obtain a yellowish translucent suspension containing invasomes. This suspension underwent ultrasound treatment (3 cycles/15 min), resulting in the formation of excellent invasomes. Free isotretinoin was separated from the invasomes using a dialysis bag. The study highlighted the influence of various formulation factors on the invasome penetration rate, emphasizing their importance as determinants. Interestingly, the concentration of eugenol did not affect the vesicle size of invasomes. However, higher concentrations of egg lecithin, characterized by a single hydrophobic chain with a polar head group, induced a strong positive curvature of the membrane, thereby increasing the size of invasome vesicles. Moreover, elevated lipid concentrations enhanced isotretinoin entrapment efficiency by providing more lipids for isotretinoin entrapment. The inclusion of eugenol also improved the solubility and incorporation of isotretinoin. Similarly, high concentrations of eugenol and lecithin exhibited high deformability of invasome vesicles. Finally, ex vivo infiltration was conducted on shaved rat skin using a Franz diffusion cell to assess invasome performance [19].

### 6.2. Delivery of anti-acne agent

Acne has remained a prevalent skin condition globally for many years. Dapsone, a highly effective pharmaceutical ingredient in leprosy treatment, exhibits promising potential in acne therapy owing to its anti-inflammatory properties. To facilitate localized drug delivery, efficient carriers are essential for transporting dapsone to targeted sites. Consequently, El-nabarawi et al. explored the preparation of dapsone-loaded invasomes using the film hydration technique, incorporating terpenes (such as limonene, cineole, citral, or fenchone) and phosphatidylcholine for treating mild to moderate acne. The study revealed that invasomes significantly enhanced dapsone skin deposition, suggesting their potential as carriers for delivering anti-acne agents. Additionally, capsaicin, a key pungent ingredient, has garnered considerable attention in the pharmaceutical realm and is widely investigated for its applications in treating oral and localized pain [20-21].

### 6.3. Anticancer drug delivery

Cancer treatment continues to pose significant challenges despite advancements in biomedicine. The high mortality rate of 4,444 deaths annually underscores the ineffectiveness of current treatment strategies, necessitating the development of more advanced alternatives. Temoporfin, a potent second-generation photosensitizer, shows promising attributes such as high tumor selectivity and residual photosensitivity within just 2 weeks. Consequently, it holds potential as an effective anticancer agent in photodynamic therapy for early or recurrent cancer. In this regard, Dragicevic-Curic et al. reported the deposition of a highly hydrophobic photosensitizer, temoporfin, within the skin layer (SC) using invasomes. They synthesized temoporfin-loaded invasomes through a mechanical dispersion method, wherein temoporfin and 1% w/v terpenes (limonene/citral/cineole) were dissolved in an ethanolic phospholipid solution (phosphatidylcholine: ethanol: 75:25 w/w). The resulting mixture underwent ultrasonication for 5 minutes after apex treatment, contributing to the development of invasome-based formulations for potential applications in cancer treatment and photodynamic therapy [2,22].

### 6.4. Immunosuppressive drug delivery

Immunosuppression stands as a key therapeutic approach for managing autoimmune diseases, although the existing repertoire of 4,444 immunosuppressive drugs presents various side effects. Nanotechnology-oriented strategies offer a promising avenue to overcome these limitations by enhancing the delivery of immunosuppressive agents to target immune system cells. By reducing the recommended dosage for therapeutic efficacy and limiting drug distribution to

non-target tissues, nanotechnology holds potential as an alternative administration route for immunosuppressants. In light of lipid vesicle substructures in drug delivery, the development of advanced nanosized vesicles emerges as a crucial focus for researchers. A review of literature underscores that cyclosporine A (CsA, CyA), characterized as a lipophilic drug with low penetration efficiency into skin layers (partition coefficient: -4000), holds promise for topical application in the treatment of psoriasis and other skin disorders [2,23-24].

### 6.5. Delivery of anti-hypertensive agent

Antihypertensive drugs play a critical role in managing high blood pressure, yet they often face challenges related to low water solubility, poor bioavailability, short biological half-life, low permeability, and a list of undesirable side effects. Effective delivery and formulation methods are pivotal in mitigating these issues. Isradipine, a calcium channel blocker commonly used for hypertension treatment, suffers from poor oral bioavailability and susceptibility to first-pass metabolism. Kamran et al. successfully developed invasomes using Phospholipon® 90G (2% w/v), β-citronella (0.1% w/v, terpene), and ethanol 10% w/v via conventional membrane hydration technology, establishing an efficient carrier for transdermal administration of isradipine. Notably, enhancing the deformability of the lipid bilayer of invasomes and disrupting the stratum corneum (SC) enhance the penetration of isradipine invasome vesicles. Consequently, the prepared isradipine invasomes follow a transdermal osmotic gradient into the SC, facilitating delivery of the antihypertensive drug to the systemic circulation. This highlights the potential of invasome delivery systems for transdermal administration of isradipine in hypertension treatment [10,22,25].

### 6.6. Antioxidant

Ferulic acid, renowned for its antioxidant properties, has garnered significant attention from researchers owing to its therapeutic effects spanning anti-cancer, anti-skin disease, anti-diabetic, anti-cardiovascular disease, and anti-inflammatory activities. Naturally occurring in many plant cell walls, ferulic acid's short elimination half-life necessitates large doses when administered regularly. To address this limitation, transdermal vesicles represent a safer option for ferulic acid delivery. Chen and colleagues prepared and compared terpene (limonene, citral, cineole-1:4.5:4.5 v/v)-based invasomes for ferulic acid delivery using a film hydration method. In comparison to conventional liposomes, ethosomes, and Tween 80-based deformable liposomes, ferulic acid invasomes exhibited superior permeability due to their deformable vesicles and the interaction of penetration enhancers with lipid lamellae and skin layers. Conventional liposomes, however, were anticipated to effectively deliver drugs to the upper layer of the skin. This study underscores the potential of invasomes as effective carriers for enhancing the transdermal delivery of ferulic acid, offering promising implications for various therapeutic applications [26].

### 6.7. Used in alopecia treatment

Advancements in dedicated treatments for alopecia are in high demand for more effective outcomes. Professional literature highlights the potential of Invasome formulations to provide long-lasting and satisfactory effects. In a recent study, authors utilized a combination of terpenes, including limonene, nerolidol, and carvone at concentrations of 0.5%, 1.5%, and 1%, respectively, to prepare invasomes of finasteride through mechanical dispersion. The finasteride-loaded invasomes demonstrated a negative charge on the surface of vesicles, attributed to the presence of ethanol, which enhanced electrostatic repulsion and bolstered the stability of the invasomal dosage form. Sonication of invasomes resulted in high rotational energies, leading to increased negative charges/potentials. These findings underscore the potential of invasome formulations as promising carriers for delivering finasteride and potentially addressing alopecia effectively [2,27-28].

## 7. Conclusion

TDDS technology is widely acknowledged as a significant advancement in mass delivery methodology, rendering it the favored modality for drug injection in transdermal delivery across diverse skin types. It effectively circumvents first-pass metabolism and other sensitivities linked with alternative drug administration routes. Through a variety of devices and TDDSs, drugs can seamlessly permeate the skin barrier and enter the systemic circulation for therapeutic effect. Many pharmaceutical active ingredients and chemical molecules exhibit high potency but limited therapeutic activity. These compounds present an opportunity for targeting through invasomes, a novel carrier known for its exceptional and tunable properties. Invasomes offer a promising approach to enhance the therapeutic effectiveness of such substances by facilitating targeted delivery and improved bioavailability. From the perspective of skin barrier properties and limitations, invasomes emerge as an outstanding alternative for dermal, transdermal, and subcutaneous applications. Their use notably enhances pharmacokinetic parameters due to drug encapsulation. The efficacy of invasome dosage forms hinges on factors such as penetration rate, the capacity to deliver actives to targeted sites, and low toxicity levels. Various considerations, including lipid to drug ratio, drug concentration, terpene ratio and

characteristics, vesicle size, and entrapment efficiency, are essential in the formulation development of invasomes. Invasomes have undergone testing for encapsulating both hydrophilic and hydrophobic drugs, thus presenting new challenges and opportunities for the advancement of novel therapies. This versatility opens avenues for the development of improved treatment modalities, offering potential solutions to various therapeutic dilemmas.

## Compliance with ethical standards

*Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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